#### Certificate of Mailing/Transmission (37 C.F.R. § 1.8(a)):

[X] Pursuant to 37 C.F.R. § 1.8, I hereby certify that this paper and all enclosures are being deposited with the United States Postal Service as first class mail on the date indicated below in an envelope addressed to the Assistant Commissioner for Patents, Washington D.C. 20231.

Dated: Majul 6, 2001

Name of Person Certifying:

Printed Name: Jocel

#### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:

Oxana Ibraghimov-Beskrovnaya et al.

Examiner:

Not Yet Assigned

Filing Date:

April 26, 2001

Serial No.:

09/830,506

Group Art Unit: Not Yet Assigned

Title:

COMPOSITIONS AND METHODS FOR TREATING POLYCYSTIC KIDNEY DISEASE

### STATEMENT REGARDING SEQUENCE LISTING UNDER 37 C.F.R.§§ 1.821-1.825

Commissioner for Patents Washington, D.C. 20231

Dear Sir:

The Applicant hereby declares that the content of the computer-readable copy of the Sequence Listing furnished herewith is the same as the written copy of the Sequence Listing.

Respectfully submitted,

Antoinette F. Konski Registration No. 34,202

Mailing Address:

McCutchen, Doyle, Brown & Enersen, LLP

Three Embarcadero Center, Suite 1800

San Francisco, CA 94111 Telephone: (650) 849-4936

Facsimile: (650) 849-4800

. . . .

# PTO/PCT Rec'd 10 AUG 2001

SEQUENCE LISTING

```
<110> Genzyme Corporation
<120> COMPOSITIONS AND METHODS FOR IDENTIFYING
 AND TREATING POLYCYSTIC KIDNEY DISEASE
<130> 126881206140
<140> PCT/US99/
<141> 1999-10-22
<150> 60/105,731
<151> 1998-10-28
<150> 60/105,876
<151> 1998-10-27
<150> 60/141,175
<151> 1999-06-25
<160> 3
<170> FastSEQ for Windows Version 3.0
<210> 1
<211> 14060
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> (135)...(13040)
<221> misc feature
<222> (2621)...(2710)
<223> epitope in the loop region of the polycystin
       transmembrane domain
<221> misc feature
\langle 222 \rangle (273\overline{4})...(3094)
<223> epitope in the loop region of the polycystin
       transmembrane domain
<221> misc feature
 \langle 222 \rangle (316\overline{6}) \dots (3300)
 <223> epitope in the loop region of the polycystin
       transmembrane domain
 <221> misc feature
 \langle 222 \rangle (336\overline{4})...(3578)
 <223> epitope in the loop region of the polycystin
       transmembrane domain
 <221> misc feature
 <222> (3623)...(3688)
 <223> epitope in the loop region of the polycystin
       transmembrane domain
 <221> misc_feature
 <222> (3710)...(3914)
 <223> epitope in the loop region of the polycystin
        transmembrane domain
 <221> misc_feature
```

<222> (3931)(4046) <223> epitope in the loop region of the polycystin transmembrane domain	-
<221> misc_feature <222> (2166)(2599) <223> epitope outside the loop region but within the polycystin transmembrane domain	
<221> misc_feature <222> (4097)(4302) <223> epitope in the loop region of the polycystin transmembrane domain	
<221> misc_feature <222> (4148)(4219) <223> epitope in the loop region of the polycystin transmembrane domain	
<221> misc_feature <222> (4220)(4302) <223> epitope in the loop region of the polycystin transmembrane domain	
<221> misc_feature <222> (27)(360) <223> epitope in the loop region of the polycystin transmembrane domain	
<221> misc_feature <222> (843)(1200) <223> Ig-like domain of polycystin	
<221> misc_feature <222> (1205)(1625) <223> Ig-like domain of polycystin	
<221> misc_feature <222> (1626)(2136) <223> Ig-like domain of polycystin	
<221> misc_feature <222> (2166)(2599) <223> isolated polypeptide	
<pre>&lt;400&gt; 1 gctcagcagc aggtcgcggc cgcagcccca tccagcccgc gcccgccatg ccgtccgcgg gccccgcctg agctgcggtc tccgcgcgg ggcgggcctg gggacggcgg ggccatgcgc gcgctgccct aacg atg ccg ccc gcc gcc gcc cgc ctg gcg ctg gcc</pre>	60 120 170
ctg ggc ctg ggc ctg tgg ctc ggg gcg ctg gcg ggg gg	218
ggc tgc ggg ccc tgc gag ccc ccc tgc ctc tgc ggc cca gcg ccc ggc Gly Cys Gly Pro Cys Glu Pro Pro Cys Leu Cys Gly Pro Ala Pro Gly 30 35 40	266
gcc gcc tgc cgc gtc aac tgc tcg ggc cgc ggg ctg cgg acg ctc ggt Ala Ala Cys Arg Val Asn Cys Ser Gly Arg Gly Leu Arg Thr Leu Gly 45 50 55 60	314
ccc gcg ctg cgc atc ccc gcg gac gcc aca gcg cta gac gtc tcc cac Pro Ala Leu Arg Ile Pro Ala Asp Ala Thr Ala Leu Asp Val Ser His	362

•		-						3						-	C1/03.	77125071
				65					70					75		-
aac c Asn I	ctg Leu	ctc Leu	cgg Arg 80	gcg Ala	ctg Leu	gac Asp	gtt Val	ggg Gly 85	ctc Leu	ctg Leu	gcg Ala	aac Asn	ctc Leu 90	tcg Ser	gcg Ala	410
ctg o	gca Ala	gag Glu 95	ctg Leu	gat Asp	ata Ile	agc Ser	aac Asn 100	aac Asn	aag Lys	att Ile	tct Ser	acg Thr 105	tta Leu	gaa Glu	gaa Glu	458
gga a Gly 1	ata Ile 110	ttt Phe	gct Ala	aat Asn	Leu	ttt Phe 115	aat Asn	tta Leu	agt Ser	gaa Glu	ata Ile 120	aac Asn	ctg Leu	agt Ser	GJ À ààà	506
aac ( Asn 1 125	ccg Pro	ttt Phe	gag Glu	tgt Cys	gac Asp 130	tgt Cys	ggc Gly	ctg Leu	gcg Ala	tgg Trp 135	ctg Leu	ccg Pro	cga Arg	tgg Trp	gcg Ala 140	554
gag ( Glu (	gag Glu	cag Gln	cag Gln	gtg Val 145	cgg Arg	gtg Val	gtg Val	cag Gln	ccc Pro 150	gag Glu	gca Ala	gcc Ala	acg Thr	tgt Cys 155	gct Ala	602
Gly	cct Pro	ggc Gly	tcc Ser 160	ctg Leu	gct Ala	ggc Gly	cag Gln	cct Pro 165	ctg Leu	ctt Leu	ggc Gly	atc Ile	ccc Pro 170	ttg Leu	ctg Leu	650
gac Asp	agt Ser	ggc Gly 175	tgt Cys	ggt Gly	gag Glu	gag Glu	tat Tyr 180	gtc Val	gcc Ala	tgc Cys	ctc Leu	cct Pro 185	gac Asp	aac Asn	agc Ser	698
Ser	ggc Gly 190	acc Thr	gtg Val	gca Ala	gca Ala	gtg Val 195	tcc Ser	ttt Phe	tca Ser	gct Ala	gcc Ala 200	cac His	gaa Glu	ggc Gly	ctg Leu	746
ctt Leu 205	cag Gln	cca Pro	gag Glu	gcc Ala	tgc Cys 210	agc Ser	gcc Ala	ttc Phe	tgc Cys	ttc Phe 215	Ser	acc Thr	ggc Gly	cag Gln	ggc Gly 220	794
ctc Leu	gca Ala	gcc Ala	ctc Leu	tcg Ser 225	gag Glu	cag Gln	ggc Gly	tgg Trp	tgc Cys 230	Leu	tgt Cys	ggg	gcg Ala	gcc Ala 235	Gin	842
ccc Pro	tcc Ser	agt Ser	gcc Ala 240	tcc Ser	ttt Phe	gcc Ala	tgc Cys	ctg Leu 245	tcc Ser	ctc Leu	tgc Cys	tcc Ser	ggc Gly 250	Pro	ccg Pro	890
cca Pro	cct Pro	cct Pro 255	Ala	ccc Pro	acc Thr	tgt Cys	agg Arg 260	Gly	ccc	acc Thr	cto Lev	ctc Leu 265	Glr	g cac n His	gtc Val	938
ttc Phe	cct Pro 270	Ala	tcc Ser	cca Pro	ggg	gcc Ala 275	Thr	ctg Leu	gto Val	g ggg Gly	280	His	gga Gly	a cct / Pro	ctg Leu	986
gcc Ala 285	tct Ser	ggc	cag Gln	cta Leu	gca Ala 290	Ala	tto Phe	cac His	ato	gct Ala 299	a Ala	c ccq a Pro	g cto Lev	c cct i Pro	gtc Val 300	1034
act Thr	gcc Ala	aca Thr	cgc Arg	tgg Trp 305	Asp	tto Phe	gga Gly	a gac / Asp	gg Gl; 31	y Sei	gc.	c gaq a Glu	g gto ı Val	g gat l As <sub>l</sub> 31	t gcc p Ala 5	1082
gct Ala	ggg	cco Pro	g gct Ala 320	a Ala	tco Ser	cat His	cgo Āro	tat g Tyr 325	. Va	g cto l Lei	g cc ı Pr	t ggg o Gly	g cg y Ar 33	g Ty	t cac r His	1130

								→								
gtg Val	acg Thr	gcc Ala 335	gtg Val	ctg Leu	gcc Ala	Leu (	999 Gly 340	gcc Ala	ggc Gly	tca Ser	gcc Ala	ctg Leu 345	ctg Leu	G] À ààà	aca Thr	1178
gac Asp	gtg Val 350	cag Gln	gtg Val	gaa Glu	Ala	gca Ala 355	cct Pro	gcc Ala	gcc Ala	ctg Leu	gag Glu 360	ctc Leu	gtg Val	tgc Cys	ccg Pro	1226
tcc Ser 365	tcg Ser	gtg Val	cag Gln	agt Ser	gac Asp 370	gag Glu	agc Ser	ctt Leu	gac Asp	ctc Leu 375	agc Ser	atc Ile	cag Gln	aac Asn	cgc Arg 380	1274
ggt Gly	ggt Gly	tca Ser	ggc Gly	ctg Leu 385	gag Glu	gcc Ala	gcc Ala	tac Tyr	agc Ser 390	atc Ile	gtg Val	gcc Ala	ctg Leu	ggc Gly 395	gag Glu	1322
gag Glu	ccg Pro	gcc Ala	cga Arg 400	gcg Ala	gtg Val	cac His	ccg Pro	ctc Leu 405	tgc Cys	ccc Pro	tcg Ser	gac Asp	acg Thr 410	gag Glu	atc Ile	1370
ttc Phe	cct Pro	ggc Gly 415	aac Asn	ggg Gly	cac His	tgc Cys	tac Tyr 420	cgc Arg	ctg Leu	gtg Val	gtg Val	gag Glu 425	aag Lys	gcg Ala	gcc Ala	1418
tgg Trp	ctg Leu 430	cag Gln	gcg Ala	cag Gln	gag Glu	cag Gln 435	tgt Cys	cag Gln	gcc Ala	tgg Trp	gcc Ala 440	Gly	gcc Ala	gcc Ala	ctg Leu	1466
gca Ala 445	Met	gtg Val	gac Asp	agt Ser	ccc Pro 450	gcc Ala	gtg Val	cag Gln	cgc Arg	ttc Phe 455	ctg Leu	gtc Val	tcc Ser	cgg Arg	gtc Val 460	1514
acc Thr	agg Arg	agc Ser	cta Leu	gac Asp 465	gtg Val	tgg Trp	atc Ile	ggc Gly	ttc Phe 470	tcg Ser	act Thr	gtg Val	cag Gln	ggg Gly 475	Val	1562
gag Glu	gtg Val	ggc Gly	cca Pro 480	gcg Ala	ccg Pro	cag Gln	ggc Gly	gag Glu 485	gcc Ala	ttc Phe	ago Ser	ctg Leu	gag Glu 490	Ser	tgc Cys	1610
cag Gln	aac Asn	tgg Trp 495	Leu	ccc Pro	Gly	gag Glu	cca Pro 500	His	cca Pro	gcc	: aca	a gcc Ala 505	GIU	g cac His	tgc Cys	1658
gtc Val	cgg Arg 510	Leu	ggg Gly	ccc Pro	acc Thr	ggg Gly 515	tgg Trp	tgt Cys	aac Asn	acc Thr	gad Asp 520	. Le	g tgo i Cys	tca Sei	a gcg Ala	1706
ecc Pro 525	His	ago Ser	tac Tyr	gtc Val	tgc Cys 530	Glu	ctg Leu	g cag i Gln	ccc Pro	gga Gly 535	y Gl	c cca y Pro	a gto o Val	g cad	g gat n Asp 540	1754
gcc Ala	gaç a Glu	g aad 1 Asr	c ctc n Leu	cto Leu 545	ı Val	gga Gly	gcg Ala	g ccc	agt Ser 550	: Gly	g ga y As	c cto p Le	g cad ı Gli	g gg n Gl; 55	a ccc y Pro 5	1802
cto Lei	g acq u Thi	g cct	t cto Lev 560	ı Ala	a caç a Glr	g cag n Gln	gac Asp	ggc Gl <sub>y</sub> 565	/ Lei	c tca i Se:	a gc r Al	c cc a Pr	g ca o Hi 57	s GI	g ccc u Pro	1850
gte Va	g gad 1 Glu	g gte u Va 57	l Met	g gta	a tto L Phe	c ccg	999 6 Gl	y Lei	g cgi u Ard	t ct g Le	g ag u Se	c cg r Ar 58	g GI	a gc u Al	c ttc a Phe	1898
ct Le	c ac u Th	c ac	g gco r Ala	c gaa a Gl	a ttt u Phe	ggç Gly	ace Th	c cad	g ga n Gl	g ct u Le	c cg u Ar	g cg g Ar	g cc g Pr	c gc	c cag a Gln	1946

								3								
	590					595					600					-
ctg Leu 605	cgg Arg	ctg Leu	cag Gln	gtg Val	tac Tyr 610	cgg Arg	ctc Leu	ctc Leu	agc Ser	aca Thr 615	gca Ala	ggg Gly	acc Thr	ccg Pro	gag Glu 620	1994
aac Asn	ggc Gly	agc Ser	gag Glu	cct Pro 625	gag Glu	agc Ser	agg Arg	tcc Ser	ccg Pro 630	gac Asp	aac Asn	agg Arg	acc Thr	cag Gln 635	ctg Leu	2042
gcc Ala	ccc Pro	gcg Ala	tgc Cys 640	atg Met	cca Pro	Gly ggg	gga Gly	cgc Arg 645	tgg Trp	tgc Cys	cct Pro	gga Gly	gcc Ala 650	aac Asn	atc Ile	2090
tgc Cys	ttg Leu	ccg Pro 655	ctg Leu	gac Asp	gcc Ala	tct Ser	tgc Cys 660	cac His	ccc Pro	cag Gln	gcc Ala	tgc Cys 665	gcc Ala	aat Asn	ggc Gly	2138
tgc Cys	acg Thr 670	tca Ser	ggg Gly	cca Pro	ggg Gly	cta Leu 675	ccc Pro	ggg Gly	gcc Ala	ccc Pro	tat Tyr 680	gcg Ala	cta Leu	tgg Trp	aga Arg	2186
gag Glu 685	ttc Phe	ctc Leu	ttc Phe	tcc Ser	gtt Val 690	gcc Ala	gcg Ala	ggg Gly	ccc Pro	ccc Pro 695	gcg Ala	cag Gln	tac Tyr	tcg Ser	gtc Val 700	2234
acc Thr	ctc Leu	cac His	ggc Gly	cag Gln 705	gat Asp	gtc Val	ctc Leu	atg Met	ctc Leu 710	cct Pro	ggt Gly	gac Asp	ctc Leu	gtt Val 715	ggc Gly	2282
ttg Leu	cag Gln	cac His	gac Asp 720	gct Ala	ggc Gly	cct Pro	ggc Gly	gcc Ala 725	ctc Leu	ctg Leu	cac His	tgc Cys	tcg Ser 730	ccg Pro	gct Ala	2330
ccc Pro	ggc Gly	cac His 735	cct Pro	ggt Gly	ccc Pro	cag Gln	gcc Ala 740	ccg Pro	tac Tyr	ctc Leu	tcc Ser	gcc Ala 745	aac Asn	gcc Ala	tcg Ser	2378
tca Ser	tgg Trp 750	ctg Leu	ccc Pro	cac His	ttg Leu	cca Pro 755	gcc Ala	cag Gln	ctg Leu	gag Glu	ggc Gly 760	act Thr	tgg Trp	gcc Ala	tgc Cys	2426
cct Pro 765	gcc Ala	tgt Cys	gcc Ala	ctg Leu	cgg Arg 770	ctg Leu	ctt Leu	gca Ala	gcc Ala	acg Thr 775	gaa Glu	cag Gln	ctc Leu	acc Thr	gtg Val 780	2474
ctg Leu	ctg Leu	ggc Gly	ttg Leu	agg Arg 785	Pro	aac Asn	cct Pro	gga Gly	ctg Leu 790	Arg	atg Met	cct Pro	ggg Gly	cgc Arg 795	Tyr	2522
gag Glu ·	gtc Val	cgg Arg	gca Ala 800	Glu	gtg Val	ggc Gly	aat Asn	ggc Gly 805	Val	tcc Ser	agg Arg	cac His	aac Asn 810	Leu	tcc Ser	2570
tgc Cys	agc Ser	ttt Phe 815	Asp	gtg Val	gtc Val	tcc Ser	cca Pro 820	Val	gct	ggg Gly	ctg Leu	cgg Arg 825	Val	atc Ile	tac Tyr	2618
cct Pro	gcc Ala 830	Pro	cgc Arg	gac	ggc Gly	cgc Arg 835	Leu	tac Tyr	gtg Val	ccc Pro	acc Thr 840	Asn	ggc Gly	tca Ser	gcc Ala	2666
ttg Leu 845	Val	cto Lev	cag Glr	gtç Val	gac Asp 850	Ser	ggt	gcc Ala	aac Asr	gcc Ala 855	Thr	g gcc Ala	acq Thi	gct Ala	cgc Arg 860	2714

WO 00/24780	6	PCT/US99/25091

WO 0	0/247	80						6						P	CT/US99/	25091
tgg Trp	cct Pro	Gly ggg	Gly	agt Ser 865	gtc Val	agc Ser	gcc Ala	Arg	ttt Phe 870	gag Glu	aat Asn	gtc Val	tgc Cys	cct Pro 875	gcc Ala	2762
ctg Leu		Ala					Gly									2810
ctg Leu	ttc Phe	tca Ser 895	gtg Val	gta Val	gca Ala	ctg Leu	ccg Pro 900	tgg Trp	ctc Leu	agt Ser	gag Glu	ggg Gly 905	gag Glu	cac His	gtg Val	2858
gtg Val	gac Asp 910	gtg Val	gtg Val	gtg Val	gaa Glu	aac Asn 915	agc Ser	gcc Ala	agc Ser	cgg Arg	gcc Ala 920	aac Asn	ctc Leu	agc Ser	ctg Leu	2906
cgg Arg 925	Val	acg Thr	gcg Ala	gag Glu	gag Glu 930	ccc Pro	atc Ile	tgt Cys	ggc Gly	ctc Leu 935	cgc Arg	gcc Ala	acg Thr	ccc Pro	agc Ser 940	2954
ccc Pro	gag Glu	gcc Ala	cgt Arg	gta Val 945	ctg Leu	cag Gln	gga Gly	gtc Val	cta Leu 950	gtg Val	agg Arg	tac Tyr	agc Ser	ccc Pro 955	gtg Val	3002
gtg Val	gag Glu	gcc Ala	ggc Gly 960	tcg Ser	gac Asp	atg Met	gtc Val	ttc Phe 965	cgg Arg	tgg Trp	acc Thr	atc Ile	aac Asn 970	gac Asp	aag Lys	3050
cag Gln	tcc Ser	ctg Leu 975	acc Thr	ttc Phe	cag Gln	aac Asn	gtg Val 980	gtc Val	ttc Phe	aat Asn	gtc Val	att Ile 985	Tyr	cag Gln	agc Ser	3098
gcg Ala	gcg Ala 990	Val	ttc Phe	aag Lys	ctc Leu	tca Ser 995	Leu	acg Thr	gcc Ala	tcc Ser	aac Asn 100	His	gtg Val	agc Ser	aac Asn	3146
	Thr		aac Asn			Val					Met					3194
ggt Gly	ctg Leu	cag Gln	gtc Val	tcc Ser 102	Thr	gtg Val	ccg Pro	gcc Ala	gtg Val 103	Leu	tcc Ser	ccc Pro	aat Asn	gcc Ala 103	Thr	3242
cta Leu	gca Ala	ctg Leu	acg Thr 104	Ala	ggc Gly	gtg Val	ctg Leu	gtg Val 104	Asp	tcg Ser	gcc Ala	gto Val	g gaç L Glu 105	ı Val	gcc Ala	3290
ttc Phe	ctg Leu	tgg Trp 105	Asn	ttt Phe	ggg	gat Asp	ggg Gly 106	Glu	cag Gln	gcc Ala	cto	cac His	s Glr	ttc Phe	cag Gln	3338
cct Pro	ccg Pro 107	Tyr	aac Asn	gag Glu	tcc Ser	ttc Phe 107	Pro	gtt Val	cca Pro	gac Asp	cco Pro	Se <sub>1</sub>	g gto r Val	g gco L Ala	c cag Gln	3386
gtg Val 108	Leu	gtg Val	gag Glu	cac His	aat Asn 109	Val	atg Met	cac His	acc Thr	tac Tyr 109	Ala	gco a Ala	c cca a Pro	a ggt o Gly	gag Glu 1100	3434
tac Tyr	ctc Leu	ctg Leu	acc Thr	gtg Val	Leu	gca Ala	tct Ser	aat Asn	gcc Ala	Phe	gaç Glu	g aad u Asi	c cte	g accurate The	g cag r Gln 15	3482
cag	gtg Val	cct	gtg	ago	gto Val	g cgc	gcc	tco Ser	cto	g cco	tco Se:	c gt r Va	g gc	t gto a Val	g ggt l Gly	353

		7		
	1120	1125	1130	-
gtg agt gac Val Ser Asp 1135	Gly Val Leu Val	gcc ggc cgg ccc gt Ala Gly Arg Pro Va 1140	c acc ttc tac ccg l Thr Phe Tyr Pro 1145	3578
cac ccg ctg His Pro Leu 1150	ccc tcg cct ggg Pro Ser Pro Gly 115	ggt gtt ctt tac ac Gly Val Leu Tyr Th 5	g tgg gac ttc ggg r Trp Asp Phe Gly 60	3626
gac ggc tcc Asp Gly Ser 1165	cct gtc ctg acc Pro Val Leu Thr 1170	cag agc cag ccg gc Gln Ser Gln Pro Al 1175	t gcc aac cac acc a Ala Asn His Thr 1180	3674
tat gcc tcg Tyr Ala Ser	agg ggc acc tac Arg Gly Thr Tyr 1185	cac gtg cgc ctg ga His Val Arg Leu Gl 1190	ng gtc aac aac acg Lu Val Asn Asn Thr 1195	3722
gtg agc ggt Val Ser Gly	gcg gcg gcc cag Ala Ala Ala Glr 1200	gcg gat gtg cgc gt Ala Asp Val Arg Va 1205	to ttt gag gag ctc al Phe Glu Glu Leu 1210	3770
cgc gga ctc Arg Gly Leu 121	Ser Val Asp Met	agc ctg gcc gtg ga Ser Leu Ala Val G 1220	ag cag ggc gcc ccc lu Gln Gly Ala Pro 1225	3818
gtg gtg gtc Val Val Val 1230	agc gcc gcg gtg Ser Ala Ala Val 123	g cag acg ggc gac a . Gln Thr Gly Asp A . 1	ac atc acg tgg acc sn Ile Thr Trp Thr 240	3866
ttc gac atg Phe Asp Met 1245	ggg gac ggc acc Gly Asp Gly Th: 1250	c gtg ctg tcg ggc c r Val Leu Ser Gly P 1255	cg gag gca aca gtg ro Glu Ala Thr Val 1260	391 ·
gag cat gtg Glu His Val	tac ctg cgg gc. Tyr Leu Arg Al. 1265	a cag aac tgc aca g a Gln Asn Cys Thr V 1270	tg acc gtg ggt gcg al Thr Val Gly Ala 1275	3962
gcc agc ccc Ala Ser Pro	gcc ggc cac ct Ala Gly His Le 1280	g gcc cgg agc ctg c u Ala Arg Ser Leu H 1285	ac gtg ctg gtc ttc is Val Leu Val Phe 1290	4010
gtc ctg gag Val Leu Glu 129	ı Val Leu Arg Va	t gaa ccc gcc gcc t 1 Glu Pro Ala Ala C 1300	gc atc ccc acg cag Cys Ile Pro Thr Gln 1305	4058
cct gac gcc Pro Asp Ala 1310	a Arg Leu Thr Al	a Tyr Val Thr Gly F	aac ccg gcc cac tac Asn Pro Ala His Tyr 1320	4106
ctc ttc gad Leu Phe Asp 1325	c tgg acc ttc gg p Trp Thr Phe Gl 1330	g gat ggc tcc tcc a y Asp Gly Ser Ser A 1335	aac acg acc gtg cgg Asn Thr Thr Val Arg 1340	4154
ggg tgc cc Gly Cys Pr	g acg gtg aca ca o Thr Val Thr Hi 1345	c aac ttc acg cgg a s Asn Phe Thr Arg S 1350	agc ggc acg ttc ccc Ser Gly Thr Phe Pro 1355	4202
ctg gcg ct Leu Ala Le	g gtg ctg tcc ac u Val Leu Ser Se 1360	c cgc gtg aac agg o er Arg Val Asn Arg o 1365	gcg cat tac ttc acc Ala His Tyr Phe Thr 1370	4250
Ser Ile Cy	c gtg gag cca ga s Val Glu Pro G 75	ng gtg ggc aac gtc Lu Val Gly Asn Val 1380	acc ctg cag cca gag Thr Leu Gln Pro Glu 1385	4298

								8								
		Phe	gtg Val				Asp					Val				4346
tgg Trp 1405	Pro	ccg Pro	ttc Phe	ccc Pro	tac Tyr 1410	Arg	tac Tyr	acc Thr	tgg Trp	gac Asp 1415	Phe	ggc Gly	acc Thr	gag Glu	gaa Glu 1420	4394
gcc Ala	gcc Ala	ccc Pro	acc Thr	cgt Arg 1425	Ala	agg Arg	ggc Gly	cct Pro	gag Glu 1430	Val	acg Thr	ttc Phe	atc Ile	tac Tyr 143	Arg	4442
			tcc Ser 1440	Tyr					Thr					Ile		4490
			gac Asp					Glu					Val			4538
		Ile	aag Lys				Ser					Leu				4586
	Leu		tct Ser			Gly					Ala					4634
			gac Asp		Gly					Pro					Āla	4682
			aca Thr 1520	Gly					Arg					Asn		4730
			agc Ser					Asn					Arg			4778
		Leu					Ser					Pro			ggg Gly	4826
	Val		ttc Phe			Ser					Ser				tat Tyr 1580	4874
					Asp					Ile					acc Thr 5	4922
				Phe					Thr					Val	acg Thr	4970
			Glu					Gln					Val		gtc Val	5018
		Leu					Gln					Gly			ttc Phe	5066
															acc Thr	5114

## WO 00/24780 PCT/US99/25091

	9	,		
1645	1650	16	55	1660
aac gtc tcc tac agc Asn Val Ser Tyr Ser 166	Trp Thr Ala	tgg agg ga Trp Arg As 1670	p Arg Gly Pro	gcc ctg 5162 Ala Leu 1675
gcc ggc agc ggc aaa Ala Gly Ser Gly Lys 1680	Gly Phe Ser	ctc acc gt Leu Thr Va 1685	g ctc gag gcc l Leu Glu Ala ( 1690	ggc acc 5210 Gly Thr
tac cat gtg cag ctg Tyr His Val Gln Leu 1695	cgg gcc acc Arg Ala Thr 1700	Asn Met Le	g ggc agc gcc u Gly Ser Ala 1705	tgg gcc 5258 Trp Ala
gac tgc acc atg gac Asp Cys Thr Met Asp 1710	ttc gtg gag Phe Val Glu 1715	cct gtg gg Pro Val Gl	g tgg ctg atg y Trp Leu Met 1720	gtg acc 5306 Val Thr
gcc tcc ccg aac cca Ala Ser Pro Asn Pro 1725	gct gcc gtc Ala Ala Val 1730	Asn Thr Se	c gtc acc ctc r Val Thr Leu 35	agt gcc 5354 Ser Ala 1740
gag ctg gct ggt ggc Glu Leu Ala Gly Gly 174	Ser Gly Val	gta tac ac Val Tyr Th 1750	r Trp Ser Leu	gag gag 5402 Glu Glu 1755
ggg ctg agc tgg gag Gly Leu Ser Trp Glu 1760	Thr Ser Glu	cca ttt ac Pro Phe Th 1765	c acc cat agc r Thr His Ser 1770	ttc ccc 5450 Phe Pro
aca ccc ggc ctg cac Thr Pro Gly Leu His 1775	ttg gtc acc Leu Val Thr i 1780	Met Thr Al	a ggg aac ccg a Gly Asn Pro 1785	ctg ggc 5498 Leu Gly
tca gcc aac gcc acc Ser Ala Asn Ala Thr 1790	gtg gaa gtg v Val Glu Val 1 1795	gat gtg ca Asp Val Gl	n Val Pro Val 1800	agt ggc 5546 Ser Gly
ctc agc atc agg gcc Leu Ser Ile Arg Ala 1805	agc gag ccc Ser Glu Pro 1810	Gly Gly Se	c ttc gtg gcg r Phe Val Ala	gcc ggg 5594 Ala Gly 1820
tcc tct gtg ccc ttt Ser Ser Val Pro Phe 182	Trp Gly Gln	ctg gcc ac Leu Ala Th 1830	r Gly Thr Asn	gtg agc 5642 Val Ser 1835
tgg tgc tgg gct gtg Trp Cys Trp Ala Val 1840	Pro Gly Gly	agc agc aa Ser Ser Ly 1845	g cgt ggc cct s Arg Gly Pro 1850	His Val
acc atg gtc ttc ccg Thr Met Val Phe Pro 1855	gat gct ggc Asp Ala Gly 1860	Thr Phe Se	c atc cgg ctc r Ile Arg Leu 1865	aat gcc 5738 Asn Ala
tcc aac gca gtc agc Ser Asn Ala Val Ser 1870	tgg gtc tca Trp Val Ser 1875	gcc acg ta Ala Thr Ty	r aac ctc acg r Asn Leu Thr 1880	gcg gag 5786 Ala Glu
gag ccc atc gtg ggc Glu Pro Ile Val Gly .1885	ctg gtg ctg Leu Val Leu 1890	Trp Ala Se	gc agc aag gtg er Ser Lys Val 195	gtg gcg 5834 Val Ala 1900
ccc ggg cag ctg gtc Pro Gly Gln Leu Val 190	His Phe Gln	atc ctg ct Ile Leu Le 1910	eu Ala Ala Gly	tca gct 5882 Ser Ala 1915

WO 00/24780 PCT/US99/25091

110 00/24/00	10		PC 170899/25091
gtc acc ttc cgc c Val Thr Phe Arg L 1920	tg cag gtc ggc ggg g eu Gln Val Gly Gly F 1925	gcc aac ccc gag gtg ct Ala Asn Pro Glu Val Le 1930	c ccc 5930 eu Pro
ggg ccc cgt ttc t Gly Pro Arg Phe S . 1935	cc cac agc ttc ccc o er His Ser Phe Pro A 1940	ege gte gga gae eae gt Arg Val Gly Asp His Va 1945	ggtg 5978 al Val
agc gtg cgg ggc a Ser Val Arg Gly L 1950	aa aac cac gtg agc t ys Asn His Val Ser 5 1955	tgg gcc cag gcg cag gt Irp Ala Gln Ala Gln Va 1960	g cgc 6026 al Arg
atc gtg gtg ctg g Ile Val Val Leu G 1965	ag gcc gtg agt ggg ( lu Ala Val Ser Gly 1 1970	ctg cag atg ccc aac to Leu Gln Met Pro Asn Cy 1975	gc tgc 6074 ys Cys 1980
Glu Pro Gly Ile A	la Thr Gly Thr Glu A	agg aac ttc aca gcc co Arg Asn Phe Thr Ala A 1990	gc gtg 6122 rg Val <sup>.</sup> 995
cag cgc ggc tct c Gln Arg Gly Ser A 2000	gg gtc gcc tac gcc rg Val Ala Tyr Ala ' 2005	tgg tac ttc tcg ctg c Trp Tyr Phe Ser Leu G 2010	ag aag 6170 ln Lys
gtc cag ggc gac t Val Gln Gly Asp S 2015	cg ctg gtc atc ctg Ser Leu Val Ile Leu 2020	tcg ggc cgc gac gtc a Ser Gly Arg Asp Val T 2025	cc tac 6218 hr Tyr
acg ccc gtg gcc c Thr Pro Val Ala A 2030	gcg ggg ctg ttg gag Ala Gly Leu Leu Glu 2035	atc cag gtg cgc gcc t Ile Gln Val Arg Ala P 2040	tc aac
gcc ctg ggc agt o Ala Leu Gly Ser ( 2045	gag aac cgc acg ctg Slu Asn Arg Thr Leu 2050	gtg ctg gag gtt cag g Val Leu Glu Val Gln A 2055	ac gcc 6314 sp Ala 2060
Val Gln Tyr Val A	gcc ctg cag agc ggc Ala Leu Gln Ser Gly 2065	ccc tgc ttc acc aac c Pro Cys Phe Thr Asn A 2070 2	gc tcg 6362 rg Ser 075
gcg cag ttt gag o Ala Gln Phe Glu i 2080	gcc gcc acc agc ccc Ala Ala Thr Ser Pro 2085	agc ccc cgg cgt gtg g Ser Pro Arg Arg Val A 2090	gee tae 6410 Ma Tyr
cac tgg gac ttt ( His Trp Asp Phe ( 2095	ggg gat ggg tcg cca Gly Asp Gly Ser Pro 2100	ggg cag gac aca gat g Gly Gln Asp Thr Asp G 2105	gag ccc 6458 Glu Pro
agg gcc gag cac Arg Ala Glu His 2110	tcc tac ctg agg cct Ser Tyr Leu Arg Pro 2115	ggg gac tac cgc gtg c Gly Asp Tyr Arg Val C 2120	eag gtg 6506 Sln Val
aac gcc tcc aac Asn Ala Ser Asn 2125	ctg gtg agc ttc ttc Leu Val Ser Phe Phe 2130	gtg gcg cag gcc acg g Val Ala Gln Ala Thr V 2135	gtg acc 6554 Val Thr 2140
Val Gln Val Leu	gcc tgc cgg gag ccg Ala Cys Arg Glu Pro 2145	gag gtg gac gtg gtc of Glu Val Asp Val Val 1 2150	ctg ccc 6602 Leu Pro 2155
ctg cag gtg ctg Leu Gln Val Leu 2160	Met Arg Arg Ser Gln	cgc aac tac ttg gag o Arg Asn Tyr Leu Glu i 5 2170	gcc cac 6650 Ala His
gtt gac ctg cgc Val Asp Leu Arg	gac tgc gtc acc tac Asp Cys Val Thr Tyr	cag act gag tac cgc	tgg gag 6698 Trp Glu

			••			-
21	75	218	80	•	2185	
					cca gcg cgt Pro Ala Arg	
gcc ctg ccc Ala Leu Pro 2205	ggc gtg Gly Val	gac gtg ago Asp Val Se: 2210	c cgg cct r Arg Pro	cgg ctg ( Arg Leu ' 2215	gtg ctg ccg Val Leu Pro	cgg 6794 Arg 2220
		Gly His Ty		Val Phe	gtc gtg tca Val Val Ser 2235	Phe
					gtg acg gtg Val Thr Val 2250	
	g Leu Val		e Glu Gly	Gly Ser	tac cgc gtg Tyr Arg Val 2265	
					tcc tac gac Ser Tyr Asp	
aac ctg ga Asn Leu Gl 2285	g gac ggc u Asp Gly	gac cag ac Asp Gln Th 2290	g ccg ctc r Pro Leu	agt ttc Ser Phe 2295	cac tgg gcc His Trp Ala	tgt 7034 Cys 2300
		Arg Glu Al		.Cys Ala	ctg aac ttt Leu Asn Phe 231	Gly
ccc cgc gg Pro Arg Gl	g agc agc y Ser Ser 2320	acg gtc ac Thr Val Th	c att cca r Ile Pro 2325	cgg gag Arg Glu	cgg ctg gcg Arg Leu Ala 2330	gct 7130 Ala
	u Tyr Thr	Phe Ser Le			gcc ggc cgc Ala Gly Arg 2345	
					ggc cgg gtg Gly Arg Val )	
att gtg to Ile Val Se 2365	c ttg gag r Leu Glu	g tgt gtg to 1 Cys Val Se 2370	c tgc aag er Cys Lys	gca cag Ala Gln 2375	gcc gtg tac Ala Val Tyr	gaa 7274 Glu 2380
		Tyr Val Ty		Gly Arg	tgc ctc aat Cys Leu Asn 239	Cys
agc agc gg Ser Ser Gl	c tcc aag y Ser Lys 2400	g cga ggg cg s Arg Gly Ar	gg tgg gct cg Trp Ala 2405	gca cgt Ala Arg	acg ttc ago Thr Phe Ser 2410	aac 7370 Asn
Lys Thr Le		Asp Glu Th			ggc agt gca Gly Ser Ala 2425	
					ggc gag gga Gly Glu Gly O	

		12				
	ctc acg gtg of Leu Thr Val 1 2450					7514
	cgc ctg tcc ( Arg Leu Ser : 2465			Leu Gly Gly		7562
	cca ctg ggc ( Pro Leu Gly 2 2480		Ala Leu T		Val His	7610
ttc gaa tgc Phe Glu Cys 2495	acg ggc tgg Thr Gly Trp	cat gac gcg His Asp Ala 2500	gag gat q Glu Asp A	gct ggc gcc Ala Gly Ala 2505	ccg ctg Pro Leu	7658
gtg tac gcc Val Tyr Ala 2510	ctg ctg ctg Leu Leu Leu	cgg cgc tgt Arg Arg Cys 2515	Arg Gln (	ggc cac tgc Gly His Cys 2520	gag gag Glu Glu	7706
	tac aag ggc Tyr Lys Gly 2530	Ser Leu Ser				7754
	agg cca cac Arg Pro His 2545					7802
gac cag ctg Asp Gln Leu	gga gcc gct Gly Ala Ala 2560	gtg gtc gcc Val Val Ala 256	a Leu Asn	agg tct ttg Arg Ser Leu 257(	Ala Ile	7850
acc ctc cca Thr Leu Pro 257	gag ccc aac Glu Pro Asn 5	ggc agc gca Gly Ser Ala 2580	a acg ggg a Thr Gly	ctc aca gtc Leu Thr Val 2585	tgg ctg Trp Leu	7898
cac ggg ctc His Gly Leu 2590	acc gct agt Thr Ala Ser	gtg ctc cca Val Leu Pro 2595	o Gly Leu	ctg cgg cag Leu Arg Gln 2600	gcc gat Ala Asp	7946
ccc cag cac Pro Gln His 2605	gtc atc gag Val Ile Glu 2610	Tyr Ser Le	g gcc ctg u Ala Leu 2615	Val Thr Val	ctg aac Leu Asn 2620	7994
gag tac gag Glu Tyr Glu	cgg gcc ctg Arg Ala Leu 2625	gac gtg gcc Asp Val Ala	g gca gag a Ala Glu 2630	ccc aag cac Pro Lys His	gag cgg Glu Arg 2635	8042
cag cac cga Gln His Arg	gcc cag ata Ala Gln Ile 2640	cgc aag aad Arg Lys Ass 26	n Ile Thr	gag act ctg Glu Thr Leu 265	Val Ser	8090
ctg agg gtc Leu Arg Val 265	cac act gtg His Thr Val	gat gac at Asp Asp Il 2660	c cag cag e Gln Gln	atc gct gct Ile Ala Ala 2665	gcg ctg Ala Leu	8138
gcc cag tgc Ala Gln Cys 2670	e atg ggg ccc Met Gly Pro	agc agg ga Ser Arg Gl 2675	g ctc gta u Leu Val	tgc cgc tcg Cys Arg Ser 2680	tgc ctg. Cys Leu	8186
aag cag acg Lys Gln Thr 2685	g ctg cac aag Leu His Lys 269	Leu Glu Al	c atg atg a Met Met 2695	Leu Ile Leu	cag gca Gln Ala 2700	8234
gag acc acc Glu Thr Thr	gcg ggc acc Ala Gly Thr	gtg acg cc Val Thr Pr	c acc gcc o Thr Ala	atc gga gac Ile Gly Asp	agc atc Ser Ile	8282

		13	1 € 176677/23071
	2705	2710	2715
Leu Asn Ile Th		c cac ctg gcc agc tcg g e His Leu Ala Ser Ser A 2725 2	
2		a gcc gag tca cca tct c y Ala Glu Ser Pro Ser A 40 2745	* *
gcg tcc cag go Ala Ser Gln A. 2750	cc tac aac ctg acc la Tyr Asn Leu Th: 2755	c tct gcc ctc atg cgc a r Ser Ala Leu Met Arg I 2760	tc ctc atg 8426 le Leu Met
cgc tcc cgc g Arg Ser Arg V 2765	tg ctc aac gag ga al Leu Asn Glu Gl 2770	g ccc ctg acg ctg gcg g u Pro Leu Thr Leu Ala G 2775	gc gag gag 8474 ly Glu Glu 2780
		g gac ccg cgg agc ctg c r Asp Pro Arg Ser Leu L 2790	
Gly Gly Ala P		c cac ttc tcc atc ccc g s His Phe Ser Ile Pro G 2805	
agc ggg gcc c Ser Gly Ala L 2815	tg gcc aac ctc ag eu Ala Asn Leu Se 28	t gac gtg gtg cag ctc a r Asp Val Val Gln Leu I 20 2825	tc ttt ctg 8618 le Phe Leu
		t ggc tat atc agc aac t e Gly Tyr Ile Ser Asn T 2840	
tcc acc aag g Ser Thr Lys V 2845	tg gcc tcg atg gc al Ala Ser Met Al 2850	a ttc cag aca cag gcc q a Phe Gln Thr Gln Ala G 2855	ggc gcc cag 8714 Gly Ala Gln 2860
atc ccc atc g Ile Pro Ile G	ag cgg ctg gcc tc lu Arg Leu Ala Se 2865	ea gag cgc gcc atc acc o er Glu Arg Ala Ile Thr V 2870	gtg aag gtg 8762 Val Lys Val 2875
Pro Asn Asn S		cc cgg ggc cac cgc agc t a Arg Gly His Arg Ser S 2885	
tcc gcc aac t Ser Ala Asn S 2895	Ser Val Val Val Gl	ng ccc cag gcc tcc gtc o n Pro Gln Ala Ser Val o 2900 2905	ggt gct gtg 8858 Gly Ala Val
gtc acc ctg g Val Thr Leu A 2910	gac agc agc aac co Asp Ser Ser Asn Pr 2915	et gcg gcc ggg ctg cat o co Ala Ala Gly Leu His 1 2920	ctg cag ctc 8906 Leu Gln Leu
aac tat acg c Asn Tyr Thr I 2925	etg ctg gac ggc ca Leu Leu Asp Gly Hi 2930	ac tac ctg tct gag gaa is Tyr Leu Ser Glu Glu 2935	cct gag ccc 8954 Pro Glu Pro 2940
tac ctg gca o Tyr Leu Ala V	gtc tac cta cac to Val Tyr Leu His Se 2945	eg gag ccc cgg ccc aat er Glu Pro Arg Pro Asn 2950	gag cac aac 9002 Glu His Asn 2955
Cys Ser Ala S	agc agg agg atc co Ser Arg Arg Ile Ai 2960	gc cca gag tca ctc cag rg Pro Glu Ser Leu Gln 2965	ggt gct gac 9050 Gly Ala Asp 2970

							14	4						10	170077723	J/1
cac His	cgg Arg	ccc Pro 2975	Tyr	acc Thr	ttc Phe	ttc Phe	att Ile 2980	Ser	ccg Pro	ggg	agc Ser	aga Arg 2985	Asp	cca Pro	gcg Ala	9098
ggg Gly	agt Ser 2990	Tyr	cat His	ctg Leu	aac Asn	ctc Leu 2995	Ser	agc Ser	cac His	ttc Phe	cgc Arg 3000	Trp	tcg Ser	gcg Ala	ctg Leu	9146
cag Gln 3005	Val	tcc Ser	gtg Val	ggc Gly	ctg Leu 3010	Tyr	acg Thr	tcc Ser	ctg Leu	tgc Cys 3015	cag Gln	tac Tyr	ttc Phe	agc Ser	gag Glu 3020	9194
gag Glu	gac Asp	atg Met	gtg Val	tgg Trp 3025	Arg	aca Thr	gag Glu	GJ À aàà	ctg Leu 3030	Leu	ccc Pro	ctg Leu	gag Glu	gag Glu 3035	Thr	9242
tcg Ser	ccc Pro	cgc Arg	cag Gln 3040	Ala	gtc Val	tgc Cys	ctc Leu	acc Thr 3045	Arg	cac His	ctc Leu	acc Thr	gcc Ala 3050	Phe	ggc Gly	9290
gcc Ala	agc Ser	ctc Leu 3055	Phe	gtg Val	ccc Pro	cca Pro	agc Ser 3060	His	gtc Val	cgc Arg	ttt Phe	gtg Val 3065	Phe	cct Pro	gag Glu	9338
ccg Pro	aca Thr 3070	Ala	gat Asp	gta Val	aac Asn	tac Tyr 3075	Ile	gtc Val	atg Met	ctg Leu	aca Thr 3080	Cys	gct Ala	gtg Val	tgc Cys	9386
ctg Leu 3085	Val	acc Thr	tac Tyr	atg Met	gtc Val 3090	Met	gcc Ala	gcc Ala	atc Ile	ctg Leu 3099	cac His	aag Lys	ctg Leu	gac Asp	cag Gln 3100	9434
ttg Leu	gat Asp	gcc Ala	agc Ser	cgg Arg 3105	Gly	cgc Arg	gcc Ala	atc Ile	cct Pro 3110	Phe	tgt Cys	gly ggg	cag Gln	cgg Arg 3115	Gly	9482
cgc Arg	ttc Phe	aag Lys	tac Tyr 3120	Glu	atc Ile	ctc Leu	gtc Val	aag Lys 3125	Thr	ggc Gly	tgg Trp	ggc Gly	cgg Arg 3130	Gly	tca Ser	9530
ggt Gly	acc Thr	acg Thr 3135	Ala	cac His	gtg Val	ggc Gly	atc Ile 3140	Met	ctg Leu	tat Tyr	ggg Gly	gtg Val 3145	Āsp	agc Ser	cgg Arg	9578
agc Ser	ggc Gly 3150	His	cgg Arg	cac His	ctg Leu	gac Asp 3155	Gly	gac Asp	aga Arg	gcc Ala	ttc Phe 3160	His	cgc Arg	aac Asn	agc Ser	9626
ctg Leu 3165	Asp	atc Ile	ttc Phe	cgg Arg	atc Ile 3170	Ala	acc Thr	ccg Pro	cac His	agc Ser 317	ctg Leu 5	ggt Gly	agc Ser	gtg Val	tgg Trp 3180	9674
aag Lys	atc Ile	cga Arg	gtg Val	tgg Trp 318	His	gac Asp	aac Asn	aaa Lys	ggg Gly 3190	Leu	agc Ser	cct Pro	gcc Ala	tgg Trp 319	Phe	9722
ctg Leu	cag Gln	cac His	gtc Val 3200	Ile	gtc Val	agg Arg	gac Asp	ctg Leu 320	Gln	acg Thr	gca Ala	cgc Arg	agc Ser 321	Ala	ttc Phe	9770
ttc Phe	ctg Leu	gtc Val 321	Asn	gac Asp	tgg Trp	ctt Leu	tcg Ser 322	Val	gag Glu	acg Thr	gag Glu	gcc Ala 322	Asn	ggg Gly	ggc Gly	9818
											gca Ala					9866

								13								
	3230					3235					3240	)				-
ttc Phe 3245	Arg	cgc Arg	ctg Leu	ctg Leu	gtg Val 3250	Ala	gag Glu	ctg Leu	cag Gln	cgt Arg 3255	Gly	ttc Phe	ttt Phe	gac Asp	aag Lys 3260	9914
cac His	atc Ile	tgg Trp	ctc Leu	tcc Ser 3265	Ile	tgg Trp	gac Asp	cgg Arg	ccg Pro 3270	Pro	cgt Arg	agc Ser	cgt Arg	ttc Phe 32 <b>7</b> 5	Thr	9962
cgc Arg	atc Ile	cag Gln	agg Arg 3280	Ala	acc Thr	tgc Cys	tgc Cys	gtt Val 3285	Leu	ctc Leu	atc Ile	tgc Cys	ctc Leu 3290	Phe	ctg Leu	10010
ggc Gly	gcc Ala	aac Asn 3295	Ala	gtg Val	tgg Trp	tac Tyr	ggg Gly 3300	Ala	gtt Val	ggc Gly	gac Asp	tct Ser 3305	Ala	tac Tyr	agc Ser	10058
acg Thr	ggg Gly 3310	His	gtg Val	tcc Ser	agg Arg	ctg Leu 3315	Ser	ccg Pro	ctg Leu	agc Ser	gtc Val 332	gac Asp 0	aca Thr	gtc Val	gct Ala	10106
gtt Val 332	Gly	ctg Leu	gtg Val	tcc Ser	agc Ser 3330	Val	gtt Val	gtc Val	tat Tyr	ccc Pro 333	Val	tac Tyr	ctg Leu	gcc Ala	atc Ile 3340	10154
ctt Leu	ttt Phe	ctc Leu	ttc Phe	cgg Arg 334	Met	tcc Ser	cgg Arg	agc Ser	aag Lys 335	Val	gct Ala	ggģ Gly	agc Ser	ccg Pro 335	Ser	10202
ccc Pro	aca Thr	cct Pro	gcc Ala 336	Gly	cag Gln	cag Gln	gtg Val	ctg Leu 336	Asp	atc Ile	gac Asp	agc Ser	tgc Cys 337	Leu	gac Asp	10250
tcg Ser	tcc Ser	gtg Val 337	Leu	gac Asp	agc Ser	tcc Ser	ttc Phe 338	Leu	acg Thr	ttc Phe	tca Ser	ggc Gly 338	Leu	cac His	gct Ala	10298
gag Glu	gcc Ala 339	Phe	gtt Val	gga Gly	cag Gln	atg Met 339	Lys	agt Ser	gac Asp	tto Lev	ttt Phe 340	ctg Leu	gat Asp	gat Asp	tct Ser	10346
aag Lys 340	Ser	ctg Leu	gtg Val	tgc Cys	tgg Trp 341	Pro	tcc Ser	ggc Gly	gag Glu	g gga Gly 341	y Thr	ctc Leu	agt Ser	tgg Trp	ccg Pro 3420	10394
gac Asp	ctg Leu	cto Leu	agt Ser	gac Asp 342	Pro	tcc Ser	att	gto Val	g ggt L Gly 343	, Sei	c aat r Ası	ctg Leu	cgg Arg	caç Glr 343	ı Leu	10442
gca Ala	cgg Arg	ggc	cag Gln 344	ı Ala	g ggc Gly	cat His	Gl <sup>2</sup>	g cto / Let 344	ı Gly	c cca y Pro	a gaq o Gli	g gag u Glu	gac Asp 345	CT?	ttc Phe	10490
tc: Se:	c ctg	gco Ala 345	a Ser	c ccc	tac Tyr	tco Ser	cct Pro	Ala	c aaa a Lys	a tc s Se	c tte r Ph	c tca e Ser 346	Ala	a tca a Sei	a gat r Asp	10538
gaa Gl:	a gad u Asp 347	Le	g ato i Ile	c caq e Gli	g cag n Glr	gto Val	Le	z gc	c gad a Gl	g gg u Gl	g gt y Va 34	l Ser	age Se:	c cc r Pr	a gcc o Ala	10586
cc Pro	o Thi	c caa	a gad n Asp	c acc	c cad r His 349	Me1	g gad	a ac	g ga r As	p Le	g ct u Le 95	c ago u Sei	c age	c ct r Le	g tcc u Ser 3500	10634

	ggg gag aag aca Gly Glu Lys Thr 3505		Leu Gln Arg		10682
gag ctg ggg Glu Leu Gly	cca ccc agc cca Pro Pro Ser Pro 3520	ggc ctg aac tgc Gly Leu Asn Trp 3525	g gaa cag ccc o o Glu Gln Pro o 3530		10730
	tcc agg aca gga Ser Arg Thr Gly				10778
ctg ccg gcc Leu Pro Ala 3550	tgg tgt gcc tcc Trp Cys Ala Ser 3555	Leu Ala His Gly	g ctc agc ctg y Leu Ser Leu 3560	ctc ctg Leu Leu	10826
gtg gct gtg Val Ala Val 3565	gct gtg gct gtc Ala Val Ala Val 3570	tca ggg tgg gtc Ser Gly Trp Val 35	l Gly Ala Ser		10874
	agt gtt gcg tgg Ser Val Ala Trp 3585		r Ser Ala Ser		10922
	ctc ggc tgg gag Leu Gly Trp Glu 3600			Ala Leu	10970
	ctg gtg gcc aag Leu Val Ala Lys 5				11018
	agc ccg gct gtg Ser Pro Ala Val 363	Thr Pro Val Se			11066
	ccc cac ggc ttt Pro His Gly Phe 3650	Ala Leu Phe Le			11114
	aag agg cta cat Lys Arg Leu His 3665				11162
	ctg ctg gtg acc Leu Leu Val Thr 3680			Ala Ser	11210
	cac gcc tac cgt His Ala Tyr Arg 5				11258
cac agc cgg His Ser Arg 3710	gcc ttc ctg gcc Ala Phe Leu Ala 371	Ile Thr Arg Se	et gag gag ctc er Glu Glu Leu 3720	tgg cca Trp Pro	11306
	cac gtg ctg ctg His Val Leu Leu 3730	Pro Tyr Val Hi			11354
cca gag ctg Pro Glu Leu	ggg ccc cca cgg Gly Pro Pro Arg 3745	ctg cgg cag gt Leu Arg Gln Va 3750	g cgg ctg cag al Arg Leu Gln	gaa gca Glu Ala 3755	11402
ctc tac cca Leu Tyr Pro	gac cct ccc ggc Asp Pro Pro Gly	ccc agg gtc ca Pro Arg Val H	ac acg tgc tcg is Thr Cys Ser	gcc gca Ala Ala	11450

	17		
3760	3765	3770	
gga ggc ttc agc acc	agc gat tac gac gtt g	gc tgg gag agt cct cac	11498
Gly Gly Phe Ser Thr	Ser Asp Tyr Asp Val G	Gly Trp Glu Ser Pro His	
3775	3780	3785	
aat ggc tcg ggg acg	tgg gcc tat tca gcg c	ecg gat ctg ctg ggg gca	11546
Asn Gly Ser Gly Thr	Trp Ala Tyr Ser Ala F	Pro Asp Leu Leu Gly Ala	
3790	3795	3800	
tgg tcc tgg ggc tcc Trp Ser Trp Gly Ser 3805	Cys Ala Val Tyr Asp S	agc ggg ggc tac gtg cag Ser Gly Gly Tyr Val Gln 3815 3820	11594
gag ctg ggc ctg agc Glu Leu Gly Leu Ser 3825	Leu Glu Glu Ser Arg A	gac cgg ctg cgc ttc ctg Asp Arg Leu Arg Phe Leu 3835	11642
cag ctg cac aac tgg	ctg gac aac agg agc o	cgc gct gtg ttc ctg gag	11690
Gln Leu His Asn Trp	Leu Asp Asn Arg Ser A	Arg Ala Val Phe Leu Glu	
3840	3845	3850	
ctc acg cgc tac agc	ccg gcc gtg ggg ctg o	cac gcc gcc gtc acg ctg	11738
Leu Thr Arg Tyr Ser	Pro Ala Val Gly Leu I	His Ala Ala Val Thr Leu	
3855	3860	3865	
cgc ctc gag ttc ccg	gcg gcc ggc cgc gcc c	ctg gcc gcc ctc agc gtc	11786
Arg Leu Glu Phe Pro	Ala Ala Gly Arg Ala 1	Leu Ala Ala Leu Ser Val	
3870	3875	3880	
cgc ccc ttt gcg ctg Arg Pro Phe Ala Leu 3885	Arg Arg Leu Ser Ala	ggc ctc tcg ctg cct ctg Gly Leu Ser Leu Pro Leu 3895 3900	11834
ctc acc tcg gtg tgc Leu Thr Ser Val Cys 390	Leu Leu Leu Phe Ala	gtg cac ttc gcc gtg gcc Val His Phe Ala Val Ala 3915	11882
gag gcc cgt act tgg	cac agg gaa ggg cgc	tgg cgc gtg ctg cgg ctc	11930
Glu Ala Arg Thr Trp	His Arg Glu Gly Arg	Trp Arg Val Leu Arg Leu	
3920	3925	3930	
gga gcc tgg gcg cgg	tgg ctg ctg gtg gcg	ctg acg gcg gcc acg gca	11978
Gly Ala Trp Ala Arg	Trp Leu Leu Val Ala	Leu Thr Ala Ala Thr Ala	
3935	3940	3945	
ctg gta cgc ctc gcc	c cag ctg ggt gcc gct	gac cgc cag tgg acc cgt	12026
Leu Val Arg Leu Ala	a Gln Leu Gly Ala Ala	Asp Arg Gln Trp Thr Arg	
3950	3955	3960	
ttc gtg cgc ggc cgc	c ccg cgc cgc ttc act	agc ttc gac cag gtg gcg	12074
Phe Val Arg Gly Arg	g Pro Arg Arg Phe Thr	Ser Phe Asp Gln Val Ala	
3965	3970	3975 3980	
cag ctg agc tcc gca Gln Leu Ser Ser Ala 398	a Ala Arg Gly Leu Ala	gcc tcg ctg ctc ttc ctg Ala Ser Leu Leu Phe Leu ) 3995	12122
ctt ttg gtc aag gct	t gcc cag cag cta cgc	ttc gtg cgc cag tgg tcc	12170
Leu Leu Val Lys Ala	a Ala Gln Gln Leu Arg	Phe Val Arg Gln Trp Ser	
4000	4005	4010	
gtc ttt ggc aag ac	a tta tgc cga gct ctg	cca gag ctc ctg ggg gtc	12218
Val Phe Gly Lys Th	r Leu Cys Arg Ala Leu	Pro Glu Leu Leu Gly Val	
4015	4020	4025	

								]	18						• `	C 17 ( G) )	/250/1
			Gly				ctc Leu 4035	Gly					Gln				12266
L	tg eu 045	Leu	gtg Val	tct Ser	tcc Ser	tgt Cys 4050	gtg Val	gac Asp	tcc Ser	ctc Leu	tgg Trp 4055	Ser	gtg Val	gcc Ala	cag Gln	gcc Ala 4060	12314
						Pro	ggg Gly				Ser					Ala	12362
					Leu		ccc Pro			Cys					Āla		12410
				Gly			cgg Arg		Gly					Arg			12458
			Ala				gag Glu 4115	Leu					Trp				12506
Ā		Tyr					ttg Leu )					Leu					12554
						Lys	gag Glu				Lys					Gly	12602
					Pro		cgc Arg			Arg					Ser		12650
				Pro			gct Ala		Ser					Pro			12698
			Ser				ggg Gly 4195	Leu					Gly				12746
T		Arg					ccc Pro					Ala					12794
						Asp	cga Arg				Ala					Tyr	12842
					Gln		cac His			Gln					Ser		12890
				Gly			cgt Arg		Pro					Arg		gca Ala	12938
I	tg Leu	ccc Pro 427	Ser	cgc Arg	ctt Leu	gcc Ala	cgg Arg 427	Ala	agt Ser	cgg Arg	ggt Gly	gtg Val 428	Asp	ctg Leu	gcc	act Thr	12986
																agc Ser	13034

WO 00/24780 PCT/US99/25091

4285 4290 4295 4300 age act tagteeteet teetggeggg ggtgggeegt ggagteggag tggacaeege 13090 Ser Thr tcagtattac tttctgccgc tgtcaaggcc gagggccagg cagaatggct qcacqtagqt 13150 tececagaga geaggeaggg geatetgtet gtetgtggge tteageactt taaagagget 13210 gtgtggccaa ccaggaccca gggtcccctc cccagctccc ttgggaagga cacagcagta 13270 ttggacggtt tctagcctct gagatgctaa tttatttccc cgagtcctca ggtacagcgg 13330 gctgtgcccg gccccaccc ctgggcagat gtcccccact gctaaggctg ctggcttcag 13390 ggagggttag cctgcaccgc cgccaccctg cccctaagtt attacctctc cagitcctac 13450 cgtactccct gcaccgtctc actgtgtgtc tcgtgtcagt aatttatatg gtgttaaaat gtqtatattt ttgtatgtca ctattttcac tagggctgag gggcctgcgc ccagagctgg cctcccccaa cacctgctgc gcttggtagg tgtggtggcg ttatggcagc ccggctgctg cttggatgcg agcttggcct tgggccggtg ctgggggcac agctgtctgc caggcactct 13690 catcacccca gaggcettgt catcetecet tgeeceagge caggtageaa gagageageg 13750 cccaggcctg ctggcatcag gtctgggcaa gtagcaggac taggcatgtc agaggacccc 13810 agggtggtta gaggaaaaga ctcctcctgg gggctggctc ccagggtgga ggaaggtgac 13870 tgtgtgtgtg tgtgtgtgcg cgcgcgcacg cgcgagtgtg ctgtatggcc caggcagcct caaggeeete ggagetgget gtgeetgett etgtgtacea ettetgtggg eatggeeget totagageet egacaceee ecaaceeeg caccaageag acaaagteaa taaaagaget 14050 gtctgactgc 14060 <210> 2 <211> 4302 <212> PRT <213> Homo sapiens <400> 2 Met Pro Pro Ala Ala Pro Ala Arg Leu Ala Leu Ala Leu Gly Leu Gly 10 Leu Trp Leu Gly Ala Leu Ala Gly Gly Pro Gly Arg Gly Cys Gly Pro 20 25 Cys Glu Pro Pro Cys Leu Cys Gly Pro Ala Pro Gly Ala Ala Cys Arg 40 Val Asn Cys Ser Gly Arg Gly Leu Arg Thr Leu Gly Pro Ala Leu Arg 55 Ile Pro Ala Asp Ala Thr Ala Leu Asp Val Ser His Asn Leu Leu Arg 70 75 Ala Leu Asp Val Gly Leu Leu Ala Asn Leu Ser Ala Leu Ala Glu Leu Asp Ile Ser Asn Asn Lys Ile Ser Thr Leu Glu Glu Gly Ile Phe Ala 100 105 Asn Leu Phe Asn Leu Ser Glu Ile Asn Leu Ser Gly Asn Pro Phe Glu 120 115 125 Cys Asp Cys Gly Leu Ala Trp Leu Pro Arg Trp Ala Glu Glu Gln Gln 130 135 140 Val Arg Val Val Gln Pro Glu Ala Ala Thr Cys Ala Gly Pro Gly Ser 150 155 160 Leu Ala Gly Gln Pro Leu Leu Gly Ile Pro Leu Leu Asp Ser Gly Cys 175 165 170 Gly Glu Glu Tyr Val Ala Cys Leu Pro Asp Asn Ser Ser Gly Thr Val 180 185 190 Ala Ala Val Ser Phe Ser Ala Ala His Glu Gly Leu Leu Gln Pro Glu 195 200 205 Ala Cys Ser Ala Phe Cys Phe Ser Thr Gly Gln Gly Leu Ala Ala Leu 220 Ser Glu Gln Gly Trp Cys Leu Cys Gly Ala Ala Gln Pro Ser Ser Ala 230 235 Ser Phe Ala Cys Leu Ser Leu Cys Ser Gly Pro Pro Pro Pro Ala 245 250 Pro Thr Cys Arg Gly Pro Thr Leu Leu Gln His Val Phe Pro Ala Ser 265 Pro Gly Ala Thr Leu Val Gly Pro His Gly Pro Leu Ala Ser Gly Gln

280

285

275

Leu Ala Ala Phe His Ile Ala Ala Pro Leu Pro Val Thr Ala Thr Arg Trp Asp Phe Gly Asp Gly Ser Ala Glu Val Asp Ala Ala Gly Pro Ala Ala Ser His Arg Tyr Val Leu Pro Gly Arg Tyr His Val Thr Ala Val Leu Ala Leu Gly Ala Gly Ser Ala Leu Leu Gly Thr Asp Val Gln Val Glu Ala Ala Pro Ala Ala Leu Glu Leu Val Cys Pro Ser Ser Val Gln Ser Asp Glu Ser Leu Asp Leu Ser Ile Gln Asn Arg Gly Gly Ser Gly Leu Glu Ala Ala Tyr Ser Ile Val Ala Leu Gly Glu Glu Pro Ala Arg Ala Val His Pro Leu Cys Pro Ser Asp Thr Glu Ile Phe Pro Gly Asn Gly His Cys Tyr Arg Leu Val Val Glu Lys Ala Ala Trp Leu Gln Ala Gln Glu Gln Cys Gln Ala Trp Ala Gly Ala Ala Leu Ala Met Val Asp Ser Pro Ala Val Gln Arg Phe Leu Val Ser Arg Val Thr Arg Ser Leu Asp Val Trp Ile Gly Phe Ser Thr Val Gln Gly Val Glu Val Gly Pro Ala Pro Gln Gly Glu Ala Phe Ser Leu Glu Ser Cys Gln Asn Trp Leu Pro Gly Glu Pro His Pro Ala Thr Ala Glu His Cys Val Arg Leu Gly Pro Thr Gly Trp Cys Asn Thr Asp Leu Cys Ser Ala Pro His Ser Tyr Val Cys Glu Leu Gln Pro Gly Gly Pro Val Gln Asp Ala Glu Asn Leu Leu Val Gly Ala Pro Ser Gly Asp Leu Gln Gly Pro Leu Thr Pro Leu Ala Gln Gln Asp Gly Leu Ser Ala Pro His Glu Pro Val Glu Val Met Val Phe Pro Gly Leu Arg Leu Ser Arg Glu Ala Phe Leu Thr Thr Ala Glu Phe Gly Thr Gln Glu Leu Arg Arg Pro Ala Gln Leu Arg Leu Gln Val Tyr Arg Leu Leu Ser Thr Ala Gly Thr Pro Glu Asn Gly Ser Glu Pro Glu Ser Arg Ser Pro Asp Asn Arg Thr Gln Leu Ala Pro Ala Cys Met Pro Gly Gly Arg Trp Cys Pro Gly Ala Asn Ile Cys Leu Pro Leu Asp Ala Ser Cys His Pro Gln Ala Cys Ala Asn Gly Cys Thr Ser Gly Pro Gly Leu Pro Gly Ala Pro Tyr Ala Leu Trp Arg Glu Phe Leu Phe Ser Val Ala Ala Gly Pro Pro Ala Gln Tyr Ser Val Thr Leu His Gly Gln Asp Val Leu Met Leu Pro Gly Asp Leu Val Gly Leu Gln His Asp Ala Gly Pro Gly Ala Leu Leu His Cys Ser Pro Ala Pro Gly His Pro Gly Pro Gln Ala Pro Tyr Leu Ser Ala Asn Ala Ser Ser Trp Leu Pro His Leu Pro Ala Gln Leu Glu Gly Thr Trp Ala Cys Pro Ala Cys Ala Leu Arg Leu Leu Ala Ala Thr Glu Gln Leu Thr Val Leu Leu Gly Leu Arg Pro Asn Pro Gly Leu Arg Met Pro Gly Arg Tyr Glu Val Arg Ala Glu Val Gly Asn Gly Val Ser Arg His Asn Leu Ser Cys Ser Phe Asp 

Val Val Ser Pro Val Ala Gly Leu Arg Val Ile Tyr Pro Ala Pro Arg Asp Gly Arg Leu Tyr Val Pro Thr Asn Gly Ser Ala Leu Val Leu Gln Val Asp Ser Gly Ala Asn Ala Thr Ala Thr Ala Arg Trp Pro Gly Gly Ser Val Ser Ala Arg Phe Glu Asn Val Cys Pro Ala Leu Val Ala Thr Phe Val Pro Gly Cys Pro Trp Glu Thr Asn Asp Thr Leu Phe Ser Val Val Ala Leu Pro Trp Leu Ser Glu Gly Glu His Val Val Asp Val Val Val Glu Asn Ser Ala Ser Arg Ala Asn Leu Ser Leu Arg Val Thr Ala Glu Glu Pro Ile Cys Gly Leu Arg Ala Thr Pro Ser Pro Glu Ala Arg Val Leu Gln Gly Val Leu Val Arg Tyr Ser Pro Val Val Glu Ala Gly Ser Asp Met Val Phe Arg Trp Thr Ile Asn Asp Lys Gln Ser Leu Thr Phe Gln Asn Val Val Phe Asn Val Ile Tyr Gln Ser Ala Ala Val Phe Lys Leu Ser Leu Thr Ala Ser Asn His Val Ser Asn Val Thr Val Asn Tyr Asn Val Thr Val Glu Arg Met Asn Arg Met Gln Gly Leu Gln Val 1010 1015 1020 Ser Thr Val Pro Ala Val Leu Ser Pro Asn Ala Thr Leu Ala Leu Thr Ala Gly Val Leu Val Asp Ser Ala Val Glu Val Ala Phe Leu Trp Asn 1050 1055 Phe Gly Asp Gly Glu Gln Ala Leu His Gln Phe Gln Pro Pro Tyr Asn · 1065 1070 Glu Ser Phe Pro Val Pro Asp Pro Ser Val Ala Gln Val Leu Val Glu His Asn Val Met His Thr Tyr Ala Ala Pro Gly Glu Tyr Leu Leu Thr Val Leu Ala Ser Asn Ala Phe Glu Asn Leu Thr Gln Gln Val Pro Val Ser Val Arg Ala Ser Leu Pro Ser Val Ala Val Gly Val Ser Asp Gly Val Leu Val Ala Gly Arg Pro Val Thr Phe Tyr Pro His Pro Leu Pro Ser Pro Gly Gly Val Leu Tyr Thr Trp Asp Phe Gly Asp Gly Ser Pro Val Leu Thr Gln Ser Gln Pro Ala Ala Asn His Thr Tyr Ala Ser Arg 1170 1175 1180 Gly Thr Tyr His Val Arg Leu Glu Val Asn Asn Thr Val Ser Gly Ala Ala Ala Gln Ala Asp Val Arg Val Phe Glu Glu Leu Arg Gly Leu Ser Val Asp Met Ser Leu Ala Val Glu Gln Gly Ala Pro Val Val Val Ser Ala Ala Val Gln Thr Gly Asp Asn Ile Thr Trp Thr Phe Asp Met Gly Asp Gly Thr Val Leu Ser Gly Pro Glu Ala Thr Val Glu His Val Tyr 1250 1255 Leu Arg Ala Gln Asn Cys Thr Val Thr Val Gly Ala Ala Ser Pro Ala Gly His Leu Ala Arg Ser Leu His Val Leu Val Phe Val Leu Glu Val Leu Arg Val Glu Pro Ala Ala Cys Ile Pro Thr Gln Pro Asp Ala Arg Leu Thr Ala Tyr Val Thr Gly Asn Pro Ala His Tyr Leu Phe Asp Trp Thr Phe Gly Asp Gly Ser Ser Asn Thr Thr Val Arg Gly Cys Pro Thr 

Val Thr His Asn Phe Thr Arg Ser Gly Thr Phe Pro Leu Ala Leu Val 1355 1360 Leu Ser Ser Arg Val Asn Arg Ala His Tyr Phe Thr Ser Ile Cys Val Glu Pro Glu Val Gly Asn Val Thr Leu Gln Pro Glu Arg Gln Phe Val 1385 1390 Gln Leu Gly Asp Glu Ala Trp Leu Val Ala Cys Ala Trp Pro Pro Phe Pro Tyr Arg Tyr Thr Trp Asp Phe Gly Thr Glu Glu Ala Ala Pro Thr Arg Ala Arg Gly Pro Glu Val Thr Phe Ile Tyr Arg Asp Pro Gly Ser Tyr Leu Val Thr Val Thr Ala Ser Asn Asn Ile Ser Ala Ala Asn Asp Ser Ala Leu Val Glu Val Gln Glu Pro Val Leu Val Thr Ser Ile Lys Val Asn Gly Ser Leu Gly Leu Glu Leu Gln Gln Pro Tyr Leu Phe Ser Ala Val Gly Arg Gly Arg Pro Ala Ser Tyr Leu Trp Asp Leu Gly Asp 1495 1500 Gly Gly Trp Leu Glu Gly Pro Glu Val Thr His Ala Tyr Asn Ser Thr Gly Asp Phe Thr Val Arg Val Ala Gly Trp Asn Glu Val Ser Arg Ser Glu Ala Trp Leu Asn Val Thr Val Lys Arg Arg Val Arg Gly Leu Val 1540 1545 1550
Val Asn Ala Ser Arg Thr Val Val Pro Leu Asn Gly Ser Val Ser Phe Ser Thr Ser Leu Glu Ala Gly Ser Asp Val Arg Tyr Ser Trp Val Leu 1570 1575 1580 Cys Asp Arg Cys Thr Pro Ile Pro Gly Gly Pro Thr Ile Ser Tyr Thr 1590 1595 Phe Arg Ser Val Gly Thr Phe Asn Ile Ile Val Thr Ala Glu Asn Glu 1605 1610 1615 Val Gly Ser Ala Gln Asp Ser Ile Phe Val Tyr Val Leu Gln Leu Ile Glu Gly Leu Gln Val Val Gly Gly Gly Arg Tyr Phe Pro Thr Asn His 1640 1645 Thr Val Gln Leu Gln Ala Val Val Arg Asp Gly Thr Asn Val Ser Tyr Ser Trp Thr Ala Trp Arg Asp Arg Gly Pro Ala Leu Ala Gly Ser Gly Lys Gly Phe Ser Leu Thr Val Leu Glu Ala Gly Thr Tyr His Val Gln Leu Arg Ala Thr Asn Met Leu Gly Ser Ala Trp Ala Asp Cys Thr Met Asp Phe Val Glu Pro Val Gly Trp Leu Met Val Thr Ala Ser Pro Asn Pro Ala Ala Val Asn Thr Ser Val Thr Leu Ser Ala Glu Leu Ala Gly 1730 1735 Gly Ser Gly Val Val Tyr Thr Trp Ser Leu Glu Gly Leu Ser Trp Glu Thr Ser Glu Pro Phe Thr Thr His Ser Phe Pro Thr Pro Gly Leu His Leu Val Thr Met Thr Ala Gly Asn Pro Leu Gly Ser Ala Asn Ala Thr Val Glu Val Asp Val Gln Val Pro Val Ser Gly Leu Ser Ile Arg Ala Ser Glu Pro Gly Gly Ser Phe Val Ala Ala Gly Ser Ser Val Pro Phe Trp Gly Gln Leu Ala Thr Gly Thr Asn Val Ser Trp Cys Trp Ala Val Pro Gly Gly Ser Ser Lys Arg Gly Pro His Val Thr Met Val Phe Pro Asp Ala Gly Thr Phe Ser Ile Arg Leu Asn Ala Ser Asn Ala Val 

Ser Trp Val Ser Ala Thr Tyr Asn Leu Thr Ala Glu Glu Pro Ile Val 1875 1880 1885 Gly Leu Val Leu Trp Ala Ser Ser Lys Val Val Ala Pro Gly Gln Leu 1895 1900 Val His Phe Gln Ile Leu Leu Ala Ala Gly Ser Ala Val Thr Phe Arg 1915 1910 Leu Gln Val Gly Gly Ala Asn Pro Glu Val Leu Pro Gly Pro Arg Phe 1930 1925 1935 Ser His Ser Phe Pro Arg Val Gly Asp His Val Val Ser Val Arg Gly 1940 1945 1950 Lys Asn His Val Ser Trp Ala Gln Ala Gln Val Arg Ile Val Val Leu 1955 1960 1965 Glu Ala Val Ser Gly Leu Gln Met Pro Asn Cys Cys Glu Pro Gly Ile 1975 1980 Ala Thr Gly Thr Glu Arg Asn Phe Thr Ala Arg Val Gln Arg Gly Ser 1990 1995 Arg Val Ala Tyr Ala Trp Tyr Phe Ser Leu Gln Lys Val Gln Gly Asp 2010 2005 Ser Leu Val Ile Leu Ser Gly Arg Asp Val Thr Tyr Thr Pro Val Ala 2025 2020 2030 Ala Gly Leu Leu Glu Ile Gln Val Arg Ala Phe Asn Ala Leu Gly Ser 2040 2045 2035 Glu Asn Arg Thr Leu Val Leu Glu Val Gln Asp Ala Val Gln Tyr Val 2055 2060 Ala Leu Gln Ser Gly Pro Cys Phe Thr Asn Arg Ser Ala Gln Phe Glu 2070 2075 Ala Ala Thr Ser Pro Ser Pro Arg Arg Val Ala Tyr His Trp Asp Phe 2085 2090 2095 Gly Asp Gly Ser Pro Gly Gln Asp Thr Asp Glu Pro Arg Ala Glu His 2105 2110 2100 Ser Tyr Leu Arg Pro Gly Asp Tyr Arg Val Gln Val Asn Ala Ser Asn 2115 2120 2125 Leu Val Ser Phe Phe Val Ala Gln Ala Thr Val Thr Val Gln Val Leu 2135 2140 Ala Cys Arg Glu Pro Glu Val Asp Val Leu Pro Leu Gln Val Leu 2150 2155 Met Arg Arg Ser Gln Arg Asn Tyr Leu Glu Ala His Val Asp Leu Arg 2170 2165 Asp Cys Val Thr Tyr Gln Thr Glu Tyr Arg Trp Glu Val Tyr Arg Thr 2180 2185 2190 Ala Ser Cys Gln Arg Pro Gly Arg Pro Ala Arg Val Ala Leu Pro Gly 2195 2200 2205 Val Asp Val Ser Arg Pro Arg Leu Val Leu Pro Arg Leu Ala Leu Pro 2220 2215 Val Gly His Tyr Cys Phe Val Phe Val Val Ser Phe Gly Asp Thr Pro 2230 2235 Leu Thr Gln Ser Ile Gln Ala Asn Val Thr Val Ala Pro Glu Arg Leu 2250 2255 2245 Val Pro Ile Ile Glu Gly Gly Ser Tyr Arg Val Trp Ser Asp Thr Arg 2265 2270 2260 Asp Leu Val Leu Asp Gly Ser Glu Ser Tyr Asp Pro Asn Leu Glu Asp 2275 2280 Gly Asp Gln Thr Pro Leu Ser Phe His Trp Ala Cys Val Ala Ser Thr 2300 2295 Gln Arg Glu Ala Gly Gly Cys Ala Leu Asn Phe Gly Pro Arg Gly Ser 2315 2310 Ser Thr Val Thr Ile Pro Arg Glu Arg Leu Ala Ala Gly Val Glu Tyr 2330 2335 2325 Thr Phe Ser Leu Thr Val Trp Lys Ala Gly Arg Lys Glu Glu Ala Thr 2350 2340 2345 Asn Gln Thr Val Leu Ile Arg Ser Gly Arg Val Pro Ile Val Ser Leu 2355 2365 2360 Glu Cys Val Ser Cys Lys Ala Gln Ala Val Tyr Glu Val Ser Arg Ser 2375 2380 Ser Tyr Val Tyr Leu Glu Gly Arg Cys Leu Asn Cys Ser Ser Gly Ser 2390 2395

Lys Arg Gly Arg Trp Ala Ala Arg Thr Phe Ser Asn Lys Thr Leu Val 2405 2410 Leu Asp Glu Thr Thr Ser Thr Gly Ser Ala Gly Met Arg Leu Val 2420 2425 Leu Arg Arg Gly Val Leu Arg Asp Gly Glu Gly Tyr Thr Phe Thr Leu 2435 2440 2445 Thr Val Leu Gly Arg Ser Gly Glu Glu Glu Gly Cys Ala Ser Ile Arg 2455 2460 Leu Ser Pro Asn Arg Pro Pro Leu Gly Gly Ser Cys Arg Leu Phe Pro 2470 2475 Leu Gly Ala Val His Ala Leu Thr Thr Lys Val His Phe Glu Cys Thr 2485 2490 Gly Trp His Asp Ala Glu Asp Ala Gly Ala Pro Leu Val Tyr Ala Leu 2500 2505 2510 Leu Leu Arg Arg Cys Arg Gln Gly His Cys Glu Glu Phe Cys Val Tyr 2520 2525 Lys Gly Ser Leu Ser Ser Tyr Gly Ala Val Leu Pro Pro Gly Phe Arg 2535 2540 Pro His Phe Glu Val Gly Leu Ala Val Val Gln Asp Gln Leu Gly 2550 2555 2560 Ala Ala Val Val Ala Leu Asn Arg Ser Leu Ala Ile Thr Leu Pro Glu 2565 2570 Pro Asn Gly Ser Ala Thr Gly Leu Thr Val Trp Leu His Gly Leu Thr 2580 2585 2590 Ala Ser Val Leu Pro Gly Leu Leu Arg Gln Ala Asp Pro Gln His Val 2605 2595 2600 Ile Glu Tyr Ser Leu Ala Leu Val Thr Val Leu Asn Glu Tyr Glu Arg 2615 2620 Ala Leu Asp Val Ala Ala Glu Pro Lys His Glu Arg Gln His Arg Ala 2630 2635 Gln Ile Arg Lys Asn Ile Thr Glu Thr Leu Val Ser Leu Arg Val His 2645 2650 Thr Val Asp Asp Ile Gln Gln Ile Ala Ala Leu Ala Gln Cys Met 2660 2665 2670 Gly Pro Ser Arg Glu Leu Val Cys Arg Ser Cys Leu Lys Gln Thr Leu 2680 2685 His Lys Leu Glu Ala Met Met Leu Ile Leu Gln Ala Glu Thr Thr Ala 2690 2695 2700 Gly Thr Val Thr Pro Thr Ala Ile Gly Asp Ser Ile Leu Asn Ile Thr 2710 2715 Gly Asp Leu Ile His Leu Ala Ser Ser Asp Val Arg Ala Pro Gln Pro 2725 2730 Ser Glu Leu Gly Ala Glu Ser Pro Ser Arg Met Val Ala Ser Gln Ala 2740 2745 2750 Tyr Asn Leu Thr Ser Ala Leu Met Arg Ile Leu Met Arg Ser Arg Val 2755 2760 2765 Leu Asn Glu Glu Pro Leu Thr Leu Ala Gly Glu Glu Ile Val Ala Gln 2770 2775 2780 Gly Lys Arg Ser Asp Pro Arg Ser Leu Leu Cys Tyr Gly Gly Ala Pro 2790 2795 Gly Pro Gly Cys His Phe Ser Ile Pro Glu Ala Phe Ser Gly Ala Leu 2805 2810 Ala Asn Leu Ser Asp Val Val Gln Leu Ile Phe Leu Val Asp Ser Asn 2820 2825 2830 Pro Phe Pro Phe Gly Tyr Ile Ser Asn Tyr Thr Val Ser Thr Lys Val 2835 2840 2845 Ala Ser Met Ala Phe Gln Thr Gln Ala Gly Ala Gln Ile Pro Ile Glu 2855 2860 Arg Leu Ala Ser Glu Arg Ala Ile Thr Val Lys Val Pro Asn Asn Ser 2870 2875 Asp Trp Ala Ala Arg Gly His Arg Ser Ser Ala Asn Ser Ala Asn Ser 2885 2890 Val Val Gln Pro Gln Ala Ser Val Gly Ala Val Val Thr Leu Asp 2905 Ser Ser Asn Pro Ala Ala Gly Leu His Leu Gln Leu Asn Tyr Thr Leu 2920

Leu Asp Gly His Tyr Leu Ser Glu Glu Pro Glu Pro Tyr Leu Ala Val Tyr Leu His Ser Glu Pro Arg Pro Asn Glu His Asn Cys Ser Ala Ser Arg Arg Ile Arg Pro Glu Ser Leu Gln Gly Ala Asp His Arg Pro Tyr Thr Phe Phe Ile Ser Pro Gly Ser Arg Asp Pro Ala Gly Ser Tyr His Leu Asn Leu Ser Ser His Phe Arg Trp Ser Ala Leu Gln Val Ser Val Gly Leu Tyr Thr Ser Leu Cys Gln Tyr Phe Ser Glu Glu Asp Met Val Trp Arg Thr Glu Gly Leu Leu Pro Leu Glu Glu Thr Ser Pro Arg Gln Ala Val Cys Leu Thr Arg His Leu Thr Ala Phe Gly Ala Ser Leu Phe Val Pro Pro Ser His Val Arg Phe Val Phe Pro Glu Pro Thr Ala Asp Val Asn Tyr Ile Val Met Leu Thr Cys Ala Val Cys Leu Val Thr Tyr Met Val Met Ala Ala Ile Leu His Lys Leu Asp Gln Leu Asp Ala Ser Arg Gly Arg Ala Ile Pro Phe Cys Gly Gln Arg Gly Arg Phe Lys Tyr Glu Ile Leu Val Lys Thr Gly Trp Gly Arg Gly Ser Gly Thr Thr Ala 31<u>3</u>0 His Val Gly Ile Met Leu Tyr Gly Val Asp Ser Arg Ser Gly His Arg His Leu Asp Gly Asp Arg Ala Phe His Arg Asn Ser Leu Asp Ile Phe Arg Ile Ala Thr Pro His Ser Leu Gly Ser Val Trp Lys Ile Arg Val Trp His Asp Asn Lys Gly Leu Ser Pro Ala Trp Phe Leu Gln His Val 3190 3195 Ile Val Arg Asp Leu Gln Thr Ala Arg Ser Ala Phe Phe Leu Val Asn 3205 3210 Asp Trp Leu Ser Val Glu Thr Glu Ala Asn Gly Gly Leu Val Glu Lys Glu Val Leu Ala Ala Ser Asp Ala Ala Leu Leu Arg Phe Arg Arg Leu Leu Val Ala Glu Leu Gln Arg Gly Phe Phe Asp Lys His Ile Trp Leu Ser Ile Trp Asp Arg Pro Pro Arg Ser Arg Phe Thr Arg Ile Gln Arg Ala Thr Cys Cys Val Leu Leu Ile Cys Leu Phe Leu Gly Ala Asn Ala Val Trp Tyr Gly Ala Val Gly Asp Ser Ala Tyr Ser Thr Gly His Val Ser Arg Leu Ser Pro Leu Ser Val Asp Thr Val Ala Val Gly Leu Val Ser Ser Val Val Tyr Pro Val Tyr Leu Ala Ile Leu Phe Leu Phe Arg Met Ser Arg Ser Lys Val Ala Gly Ser Pro Ser Pro Thr Pro Ala Gly Gln Gln Val Leu Asp Ile Asp Ser Cys Leu Asp Ser Ser Val Leu Asp Ser Ser Phe Leu Thr Phe Ser Gly Leu His Ala Glu Ala Phe Val Gly Gln Met Lys Ser Asp Leu Phe Leu Asp Asp Ser Lys Ser Leu Val Cys Trp Pro Ser Gly Glu Gly Thr Leu Ser Trp Pro Asp Leu Leu Ser Asp Pro Ser Ile Val Gly Ser Asn Leu Arg Gln Leu Ala Arg Gly Gln Ala Gly His Gly Leu Gly Pro Glu Glu Asp Gly Phe Ser Leu Ala Ser 

Pro Tyr Ser Pro Ala Lys Ser Phe Ser Ala Ser Asp Glu Asp Leu Ile Gln Gln Val Leu Ala Glu Gly Val Ser Ser Pro Ala Pro Thr Gln Asp Thr His Met Glu Thr Asp Leu Leu Ser Ser Leu Ser Ser Thr Pro Gly Glu Lys Thr Glu Thr Leu Ala Leu Gln Arg Leu Gly Glu Leu Gly Pro Pro Ser Pro Gly Leu Asn Trp Glu Gln Pro Gln Ala Ala Arg Leu Ser Arg Thr Gly Leu Val Glu Gly Leu Arg Lys Arg Leu Leu Pro Ala Trp Cys Ala Ser Leu Ala His Gly Leu Ser Leu Leu Leu Val Ala Val Ala Val Ala Val Ser Gly Trp Val Gly Ala Ser Phe Pro Pro Gly Val Ser Val Ala Trp Leu Leu Ser Ser Ser Ala Ser Phe Leu Ala Ser Phe Leu Gly Trp Glu Pro Leu Lys Val Leu Leu Glu Ala Leu Tyr Phe Ser Leu Val Ala Lys Arg Leu His Pro Asp Glu Asp Asp Thr Leu Val Glu Ser Pro Ala Val Thr Pro Val Ser Ala Arg Val Pro Arg Val Arg Pro Pro His Gly Phe Ala Leu Phe Leu Ala Lys Glu Glu Ala Arg Lys Val Lys Arg Leu His Gly Met Leu Arg Ser Leu Leu Val Tyr Met Leu Phe Leu Leu Val Thr Leu Leu Ala Ser Tyr Gly Asp Ala Ser Cys His Gly His Ala Tyr Arg Leu Gln Ser Ala Ile Lys Gln Glu Leu His Ser Arg Ala 3700 3705 3710 Phe Leu Ala Ile Thr Arg Ser Glu Glu Leu Trp Pro Trp Met Ala His 3715 3720 3725 Val Leu Leu Pro Tyr Val His Gly Asn Gln Ser Ser Pro Glu Leu Gly 3730 3740 Pro Pro Arg Leu Arg Gln Val Arg Leu Gln Glu Ala Leu Tyr Pro Asp Pro Pro Gly Pro Arg Val His Thr Cys Ser Ala Ala Gly Gly Phe Ser Thr Ser Asp Tyr Asp Val Gly Trp Glu Ser Pro His Asn Gly Ser Gly Thr Trp Ala Tyr Ser Ala Pro Asp Leu Leu Gly Ala Trp Ser Trp Gly Ser Cys Ala Val Tyr Asp Ser Gly Gly Tyr Val Gln Glu Leu Gly Leu Ser Leu Glu Glu Ser Arg Asp Arg Leu Arg Phe Leu Gln Leu His Asn Trp Leu Asp Asn Arg Ser Arg Ala Val Phe Leu Glu Leu Thr Arg Tyr Ser Pro Ala Val Gly Leu His Ala Ala Val Thr Leu Arg Leu Glu Phe Pro Ala Ala Gly Arg Ala Leu Ala Ala Leu Ser Val Arg Pro Phe Ala Leu Arg Arg Leu Ser Ala Gly Leu Ser Leu Pro Leu Leu Thr Ser Val Cys Leu Leu Phe Ala Val His Phe Ala Val Ala Glu Ala Arg Thr Trp His Arg Glu Gly Arg Trp Arg Val Leu Arg Leu Gly Ala Trp Ala Arg Trp Leu Leu Val Ala Leu Thr Ala Ala Thr Ala Leu Val Arg Leu Ala Gln Leu Gly Ala Ala Asp Arg Gln Trp Thr Arg Phe Val Arg Gly Arg Pro Arg Arg Phe Thr Ser Phe Asp Gln Val Ala Gln Leu Ser Ser 

Ala Ala Arg Gly Leu Ala Ala Ser Leu Leu Phe Leu Leu Leu Val Lys 3990 3995 Ala Ala Gln Gln Leu Arg Phe Val Arg Gln Trp Ser Val Phe Gly Lys 4005 4010 Thr Leu Cys Arg Ala Leu Pro Glu Leu Leu Gly Val Thr Leu Gly Leu 4020 4025 4030 Val Val Leu Gly Val Ala Tyr Ala Gln Leu Ala Ile Leu Leu Val Ser 4040 Ser Cys Val Asp Ser Leu Trp Ser Val Ala Gln Ala Leu Leu Val Leu 4050 4055 4060 Cys Pro Gly Thr Gly Leu Ser Thr Leu Cys Pro Ala Glu Ser Trp His 4070 4075 Leu Ser Pro Leu Leu Cys Val Gly Leu Trp Ala Leu Arg Leu Trp Gly 4085 4090 4095 Ala Leu Arg Leu Gly Ala Val Ile Leu Arg Trp Arg Tyr His Ala Leu 4100 4105 4110 Arg Gly Glu Leu Tyr Arg Pro Ala Trp Glu Pro Gln Asp Tyr Glu Met 4120 Val Glu Leu Phe Leu Arg Arg Leu Arg Leu Trp Met Gly Leu Ser Lys 4135 4130 4140 Val Lys Glu Phe Arg His Lys Val Arg Phe Glu Gly Met Glu Pro Leu 4150 4155 Pro Ser Arg Ser Ser Arg Gly Ser Lys Val Ser Pro Asp Val Pro Pro 4165 4170 4175 Pro Ser Ala Gly Ser Asp Ala Ser His Pro Ser Thr Ser Ser Sln 4180 4185 4190 Leu Asp Gly Leu Ser Val Ser Leu Gly Arg Leu Gly Thr Arg Cys Glu 4195 4200 Pro Glu Pro Ser Arg Leu Gln Ala Val Phe Glu Ala Leu Leu Thr Gln 4215 4220 Phe Asp Arg Leu Asn Gln Ala Thr Glu Asp Val Tyr Gln Leu Glu Gln 4230 4235 Gln Leu His Ser Leu Gln Gly Arg Arg Ser Ser Arg Ala Pro Ala Gly 4245 4250 Ser Ser Arg Gly Pro Ser Pro Gly Leu Arg Pro Ala Leu Pro Ser Arg 4260 4265 Leu Ala Arg Ala Ser Arg Gly Val Asp Leu Ala Thr Gly Pro Ser Arg 4275 4280 Thr Pro Leu Arg Ala Lys Asn Lys Val His Pro Ser Ser Thr

<210> 3

<211> 34

<212> DNA

<213> Homo sapiens

<400> 3

gtaatacgac tcactatagg gcgagccacc atgg